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			OFFICE (DO/EO/US)	056291-5075
				U.S. Application No. 10/069356 Unassigned
Intern	otional Ann	NG A FILING	UNDER 35 U.S.C. § 371	
mem	анонаі Арр	meadon. No.	International Filing Date	Priority Date Claimed
<u>P</u>	CT/GB00/0	3192	August 21, 2000	August 27, 1999
Title o	of Invention	: CATALYS	Γ FOR PAUSON-KHAND RE	ACTION
Applio	cants For E	O/EO/US: Alex	Christian COMELY, Sue Eliz	zabeth GIBSON and Neil James HALES
Ap	plicants her	rewith submit to	o the United States Designated	/Elected Office (DO/EO/US) the following items and
other i	information	:	o the Office States Designated	Do Ecologica (Do Ecolog) the following items and
1.	\boxtimes		ST submission of items conce	rning a filing under 35 U.S.C. § 371.
2.		This is a SEC	COND or SUBSEQUENT sub	mission of items concerning a filing under
	_	35 U.S.C. § 3	371.	and the state of t
3.				nination procedures (35 U.S.C. § 371(f)) at
		any time rath	er than delay examination unt	il the expiration of the applicable time limit
		set in 35 U.S	.C. § 371(b) and PCT Articles	22 and 39(1).
4.	\boxtimes	A proper De	mand for International Prelimi	nary Examination was made by the 19th
		month from	the earliest claimed priority da	te.
5.	\boxtimes	A copy of the	e International Application as	filed (35 U.S.C. § 371(c)(2))
		a. 🗌	is transmitted herewith (r	equired only if not transmitted by the
			International Bureau).	•
		b. 🔼	has been transmitted by the	he International Bureau.
		c	is not required, as the app	lication was filed in the United States
	_		Receiving Office (RO/US	S).
6.	Ц	A translation	of the International Application	on into English (35 U.S.C. § 371(c)(2)).
7.	\bowtie	Amendments	s to the claims of the Internatio	nal Application under PCT Article 19
		(35 U.S.C. §		
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		b	have been transmitted by	
		c. 🛚	have not been made; how	ever, the time limit for making such
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0		d	have not been made and v	
8.			of the amendments to the clair	ms under PCT Article 19 (35 U.S.C.
0		§ 371(c)(3)).	-1	II G G A 6544 A (A)
9. 10.	H	An oath or de	eclaration of the inventors (35)	U.S.C. § 3/1(c)(4)).
10.	Ш	A translation	of the annexes to the international and the second of the	onal Preliminary Examination Report
Items '	11 to 11 h		rticle 36 (35 U.S.C. § 371(c)(5 other document(s) or inform:	
11.		An Information	on Disclosure Statement under	27 CED \$ 1.07 and \$ 1.00
12.	Ħ	An Information Disclosure Statement under 37 C.F.R. § 1.97 and § 1.98.		
12.		An assignment document for recording. A separate cover sheet in compliance with 37 C.F.R. § 3.28 and § 3.31 is included.		
13.			liminary amendment.	
	Ħ	A SECOND	or SUBSEQUENT preliminary	z amendment
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		a. WO 01/16		
		b. PCT/IB/30		
			nal Search Report	
		d. PTO Form		
		e. PCT/IB/40	9	

Unassigned PCT/GB00/03192 15. The following fees are submitted: Basic National Fee (37 C.F.R. § 1.492(a)(1)-(5)):			
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Search Report has been prepared by the EPO or JPO\$890.00			
International preliminary examination fee paid to			
USPTO (37 C.F.R. § 1.482)\$710.00			
No international preliminary examination fee paid to			
USPTO (37 C.F.R. § 1.482) but international search fee			
paid to USPTO (37 C.F.R. § 1.445(a)(2))\$740.00			
Neither international preliminary examination fee			
(37 C.F.R. § 1.482) nor international search fee			
(37 C.F.R. § 1.445(a)(2)) paid to USPTO\$1,040.00			
International preliminary examination fee paid to USPTO			
(37 C.F.R. § 1.482) and all claims satisfied provisions			
of PCT Article 33(2)-(4)\$100.00			
ENTER APPROPRIATE BASIC FEE AMOUNT = 1980	90.00		
urcharge of \$130.00 for furnishing the oath or declaration later than	20.00		
☐ 20 ☐ 30 months from the earliest claimed priority date			
37 C.F.R. § 1.492(e)).			
<u>Claims</u> <u>Number Filed</u> <u>Number Extra</u> <u>Rate</u>			
Total Claims 8 - 20 = 0 X \$18.00 \$			
[-11(01)	84.00		
Multiple dependent claim(s) (if applicable) + \$280.00 \$	04.00		
TOTAL OF ABOVE CALCULATIONS \$			
Reduction by ½ for filing by small entity, if applicable.			
Verified Small Entity statement must also be filed. (Note 37 C.F.R. §§ 1.9, 1.27, 1.28)	ž.		
SUBTOTAL = \$			
Processing fee of \$130.00 for furnishing the English translation later			
than 20 30 months from the earliest claimed priority date (37 C.F.R. § 1.492(f)).	\$		
	974.00		
Fee for recording the enclosed assignment (37 C.F.R. § 1.21(h)).	774.00		
The Assignment must be accompanied by an appropriate cover sheet			
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Amount to be refunded \$	714.00		
	974.00		
a. A check in the amount of \$ to cover the above fees is enclosed.	374.00		
b. Please charge my Deposit Account No. 50-0310 in the amount of \$974.00			
to cover the above fees. A duplicate copy of this sheet is enclosed.			
c. Except for issue fees payable under 37 C.F.R. § 1.130, the Commissioner is hereby			
authorized by this paper to charge any additional fees during the entire pendency of this			
application including fees due under 37 C.F.R. § 1.16 and § 1.17 which may be required, or			
credit any overpayment to Deposit Account No. 50(0310.)			
ustomer No. 09629			
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CATALYST FOR PAUSON-KHAND REACTION

The invention relates to the use of an immobilised transition metal carbonyl complex as a catalyst in the Pauson-Khand reaction and to processes using such a catalyst.

The reaction between an π-alkynedicobalt hexacarbonyl complex, an alkene, and carbon monoxide to produce a cyclopentenone is generally referred to as the Pauson-Khand reaction (P.L. Pauson, *Tetrahedron*, 1985, 41, 5860) (Scheme 1).

$$(CO)_3 Co Co(CO)_3$$
 X
 Y
 Y
 Y
 Y
 Y
 X
 X
 Y
 Y

Scheme 1: Pauson-Khand reaction

The products of the Pauson-Khand reaction are in general chiral except in the case of certain symmetrical alkenes (X=X' and Y=Y'). If the components of the reaction are racemic or prochiral then chiral cyclopentenones produced by the reaction are produced in racemic form.

The reaction succeeds for a wide range of substrates with the exception of tetrasubstituted alkenes, which are normally unreactive. The stereochemistry (e.g. M.E. Kraft, *J. Amer. Chem. Soc.*, 1988, **110**, 968) and regiochemistry (e.g. K.H. Dotz and M. Popall, *Tetrahedron*,1985, **41**, 5797) of the reaction have been the subject of investigation, for instance in the case of unsymmetrical alkynes the larger substituent (e.g. R') generally forms the substituent at the α carbon of the cyclopentenone.

In cases where the alkyne and alkene are both part of the same organic molecule the reaction forms two rings and where the olefin is itself cyclic tricyclic products are easily produced so that the reaction can give products of great complexity.

Accordingly the reaction is valuable because it makes complex organic molecules from 5 simple components and these complex molecules are valuable *per se* or as intermediates for the production of high value-added products such as pharmaceuticals and fine chemicals.

Mixtures of an alkyne, an alkene, and carbon monoxide can also be converted *in situ* into π-alkynedicobalt hexacarbonyl complexes using stoichiometric amounts of dicobalt octacarbonyl or its tricobalt or tetracobalt homologues as part of the synthetic route leading to cyclopentenones.

Substoichiometric amounts of dicobalt octacarbonyl or π-alkynedicobalt hexacarbonyl have also been used to catalyse the formation of cyclopentenones from alkynes, alkenes, and carbon monoxide (e.g. I.U. Khand, G.R. Knox, P.L. Pauson, W.E. Watts, and M.I. Foreman, *J. Chem. Soc., Perkin Trans. I*, 1973, 977; D.B. Belanger, D.J.R. O'Mahoney and T. Livinghouse, 15 *Tetrahedron Lett.*, 1998, 39, 7637; and D.B. Belanger and T. Livinghouse, *Tetrahedron Lett.*, 1998, 39, 7641).).

Derivatives of π-alkynedicobalt hexacarbonyl complexes such as π-alkynedicobaltcarbonylphosphine complexes have been used in the Pauson-Khand reaction (P. Bladon, P.L. Pauson, H. Brunner and R. Eder, *J. Organometal. Chem.*, 1988, 355, 449) and catalysis of the Pauson-Khand reaction using dicobalt octacarbonyl has been performed in the presence of added ligands such as phosphites and phosphines (N. Jeong, S.H. Hwang, Y. Lee and Y.K. Chung, *J. Amer. Chem. Soc.*, 1994, 116, 3159). Heterobimetallic analogues in which a cobalt atom has been replaced by molybdenum are also known (D.T. Rutherford and S.D.R. Christie *Tetrahedron Lett.*, 1998, 39, 9805).

We use the term "Pauson-Khand" reaction to include all reactions between carbon monoxide, alkenes, and alkynes that are promoted by transition metal complexes and that lead to cyclopentenone formation. Specifically, and preferably, by the use of the term "Pauson-Khand" reaction we refer to Scheme 1, wherein Co is cobalt or any other transition metal as described

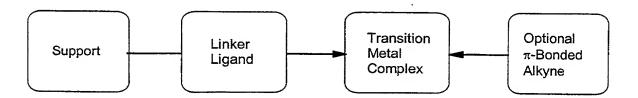
herein, R and R', X and X', Y and Y' may be the same or different and wherein X and R may be joined together, or X and Y together form a ring system.

Although the Pauson-Khand reaction produces useful products it suffers from a number of drawbacks. Dicobaltoctacarbonyl and its analogues are volatile, toxic, and unstable both to loss of carbon monoxide and to aerial oxidation. Accordingly the cobalt carbonyl reagent poses hazards in storage, use, disposal, and product purification. For best results the commercial reagent often requires rigorous purification immediately before use (e.g. "Impure samples of commercial Co₂(CO)₈ must be rigorously purified by recrystallisation from degassed HPLC grade hexane or room temperature sublimation at 50 mTorr immediately prior to use". T.

Livinghouse, *Tetrahedron Lett*, 1998, 39, 7637). In addition, generally, the cyclopentenone product may retain metal impurities, especially when used stoicheometrically.

We have recently described the use of immobilised transition metal complexes as traceless linkers for unsaturated organic molecules (WO00/007966). A class of immobilised π-alkynedicobalt hexacarbonyl complexes used as traceless linkers for alkyne derivatives were disclosed, in which an alkyne is immobilised using its π-alkynedicobalt hexacarbonyl complex as a traceless link, the alkyne or its derivative would can be easily liberated at the end of a sequence of stoichiometric steps.

We have now found that immobilised cobalt carbonyl complexes prepared for use as traceless linkers are members of an advantageous class of catalysts that promote the Pauson-20 Khand reaction. The invention is illustrated below.



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Where the Transition Metal Complex is drawn from the group of transition metal-ligand complexes known to promote the Pauson-Khand reaction and is preferably a cobalt carbonyl or coablat complex derivative thereof.

For instance, the invention is illustrated below (Catalyst A) where the support is a cross linked polystyrene resin, the linker ligand is a diphenylphosphine, and the transition metal complex is derived from dicobalt octacarbonyl. The representation of Catalyst A is schematic and is not intended to define the chemical constitution or the bonding of the catalytically active species.

The method of the invention offers considerable advantages. It is safe and convenient to use at all stages of the operation. The immobilised catalysts may be prepared in active form from commercially available precursors such as dicobalt octacarbonyl (Strem Chemical Co. Inc.) and they retain their activity for longer than their analogues that are not immobilised. The immobilised catalysts are not volatile and are easier to contain than their analogues that are not immobilised. Accordingly they are safer to use, store, and transport. The immobilised catalyst may also be easily recovered from the reaction, for example, by filtration so that valuable catalysts may be recovered for reuse, potential environmental contaminants may be easily eliminated, and the product may be separated from potentially noxious transition metal carbonyl contaminants. Because the catalyst may be easily recovered for reuse the method of the invention

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enables the economic use of costly transition metal complexes designed to confer special benefits such as the production of enantiomerically pure or enriched cyclopetenones.

An example of the use of an immobilised catalyst is given in Scheme 2.

Presented as a first feature of the invention is the use of an immobilised cobalt carbonyl complex as a catalyst in a Pauson-Khand reaction.

The immobilised π -alkynecobaltcarbonyl complex may also be activated as a catalyst for the Pauson-Khand reaction by prior conversion into an alkyne complex. The alkyne may be one which is the same as the alkyne reagent used in the Pauson-Khand reaction or may be one which is readily displaced by the alkyne reagent used in the Pauson-Khand reaction and therefore will exchange with the alkyne reagent to form a complex with the cobalt.

Presented as a further feature of the invention is the use of an immobilised π -alkynecobalt carbonyl complex as a catalyst for the Pauson-Khand reaction.

A further feature is the use of immobilised analogues and derivatives of cobalt carbonyls and their alkyne complexes as catalysts in a Pauson-Khand reaction.

As discussed above, depending upon the starting alkene starting material, chiral centres may be found in the cyclopentenone product. However, typically, Pauson-Khand reactions produce racemic mixtures of any product with a chiral centre. In the prior art it is suggested that carbonylmetal complexes can be generated as catalysts for the Pauson-Khand reaction which will produce enatiomerically enriched products. This would be extremely valuable in the

20 pharmaceutical and specialty chemical fields since enatiomerically pure products are desired. However, the drawbacks mentioned above make this prohibitively expensive. In addition any extra effort and expense in producing a complex chiral catalyst would be wasted since little of the original starting catalyst would be available for subsequent reactions. In the present invention the ability to recover a significant amount of catalyst allows increased and rewarding efforts to be made in preparing catalysts for the Pauson-Khand reaction which are able to produce enatiomerically enriched products.

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The Pauson-Khand reaction is not limited to complexes of cobalt: other transition metals that are able to form π -alkyne and π -alkene transitionmetalcarbonyl complexes in the presence of carbon monoxide, alkynes and alkenes are also able to promote cyclopentenone formation from carbon monoxide, alkynes, and alkenes. Such metals form part of the invention described herein 5 and include other metals of the cobalt group, namely rhodium and iridium, from other groups such as; tungsten and molybdenum (T.R. Hoye, J.A. Suriano Organometallics, 1992, 11, 2044), titanium (N.M. Kablaoui, F.A. Hicks, and S.L. Buchwald J. Amer. Chem. Soc., 1996, 118, 5818), iron and ruthenium (T. Morimoto, N. Chatani, Y. Fukumoto, and S. Murai, J. Org. Chem., 1997, 62, 3762).

Further features of the invention are the immobilised catalysts, their uses and processes, as defined above or below, in which one [or both] of the cobalt atoms is replaced by a metal independently selected from a transition group metal, preferably of the same periodic group as cobalt. Transition metals that are suitable for use in Pauson-Khand reaction are known to the skilled person or may be tested for their ability to catalyse a Pauson-Khand reaction. Suitable 15 transition metals from the same periodic group as cobalt are selected from; rhodium and iridium; transition metals of other periodic groups include; titanium, ruthenium, tungsten, molybdenum, nickel, and iron.

Immobilised heterobimetallic carbonyl complexes may be formed and these represent a further novel feature of the invention as being particularly useful for producing chiral catalysts of 20 value in the production of enatiomerically enriched cyclopentenone products.

A further feature is the use of a resolved or partially resolved cobalt carbonyl complex wherein one of the cobalt atoms is replaced by different transition metal in a Pauson-Khand reaction to produce, preferably, a resolved or partly resolved product.

A further feature of the invention is a process for the preparation of a cyclopentenone 25 compound or analogue thereof in a Pauson-Khand reaction, which comprises either; reacting an alkyne, an alkene, and carbon monoxide in the presence of an immobilised cobaltcarbonyl catalyst; or reacting an alkyne, an alkene, and carbon monoxide in the presence of an immobilised alkynecobaltcarbonyl catalyst.

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By use of the term "analogue" we mean a compound which is formed by a Pauson-Khand reaction a cyclopentenone ring.

A further feature is the use of resolved or partially resolved complexes in which the cobalt carbonyl complex [e.g. LCo₂CO₅alkyne] or a transition metal complex analogue, to prepare a product that is resolved or partially resolved.

The linking group can be any functional group capable of complexing with the transition metal and joining to the support. The linker group is preferably selected from those ligands known to form a strong bond to the transition metal. Suitable ligands include phosphines,

10 phosphites, and isonitriles. Chiral cobalt carbonyl complexes may be prepared by introducing a chiral centre into the linking ligand that connects the support and cobalt.

A further feature is the use of a resolved or partially cobaltcarbonyl complex containing a chiral centre within the ligand linking the cobalt to the immobilised support, in a Pauson-Khand reaction to give a product that is, preferably, resolved or partially resolved.

The support to which the catalyst is immobilised may be insoluble, such as a polymer or resin, or soluble, such as a polyethylene glycol (PEG) which can be selectively precipitated as required, or fluorous phases, which show temperature dependent immiscibility with common organic solvents.

In addition the alkyne and alkene reagent for the Pauson-Khand reaction may form part of 20 the same molecule.

The cobalt carbonyl complex may be prepared by one of the following alternative steps:

- (1) bonding the cobalt complex, which has bound to it through a π -complex bond an alkyne, with the support, where either the cobalt complex or support has a linker group capable of forming a bond or interaction between the cobalt complex and the support;
- 25 (2) bonding the alkyne with the cobalt complex, which is bound to the support via a linker, by forming a π -complex between the supported cobalt and the alkyne

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(3) converting an organic molecule attached to the cobalt metal, which is bound to the support via the linker group, to form a π -complex between the supported cobalt complex and the alkyne.

The invention is illustrated below by the following example where the precursor to the catalytically active species is believed to be polymer-bound dicobalthexacarbonyl, but we do not wish to be limited by this theory.

An example of the use of an immobilised catalyst is given in Scheme 2.

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Scheme 2

Catalyst A precursor resin

Polystyrene-bound diphenylphosphine (2 g, 3.2 mmolP) was suspended at ambient temperature in anhydrous tetrahydrofuran (THF) (15 cm³) and a solution of octacarbonyldicobalt(0) (1.1g, 3.2mmol) in anhydrous THF (5 cm³) was added *via* filter cannula. After 1.5h under constant nitrogen agitation, the mixture was filtered and the resin was washed with alternate aliquots of THF and diethyl ether until the filtrate became colourless. The resulting deep purple beads were dried *in vacuo* to afford the resin complex (2.84 g, 1.0 mmol[Co₂(CO)_x]g⁻¹); ν_{max}(nujol)/cm⁻¹ 2074w, 2015msh, 1995ssh, 1979s, 1951m, 1872s; δ_P (145.8 MHz)(D₂O capillary lock) 32 [polymer-P(O)Ph₂, 10%], 67 [polymer-(PPh₂)_yCo₂(CO)_x, 90%].

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EXAMPLES

Example of catalysis

2,3,3a,4-Tetrahydro-2-[(4-methylphenyl)sulfonyl]-cyclopenta[c]pyrrol-5(1H)-one.

5 To a suspension of the catalyst A precursor resin, shown above {24mg, 0.025mmol[Co₂(CO)_m]} in anhydrous THF(5cm³) was added *N*-(2-propenyl)-*N*-(2-propynyl)-4-methylphenylsulfonamide (125 mg, 0.5 mmol) and the resulting mixture was heated to 65 °C under an atmosphere of CO (50 mbar). After 48h the mixture was filtered, the resin was washed with THF (2 x 1 cm³) and the combined filtrates were concentrated *in vacuo*. ¹H-NMR spectroscopy of the pale yellow residue indicated a 1:1 mixture of starting material and product and no by-products. Purification by flash chromatography (SiO₂, 20% EtOAc/hexane) gave the title compound (46mg, 0.167mmol, 33%) as a white solid; mp 147-149 °C; ν_{max}(CH₂Cl₂)/cm⁻¹ 3058, 1716, 1651, 1350, 1164, 1094, 673; δ_H (360 MHz)(CDCl₃) 1.96-2.02 (1 H, m), 2.32 (3 H, s, CH₃), 2.48-2.58 (2 H, m), 3.01-3.36(1 H, m), 3.93-3.98 (2 H, m), 4.27 (1 H, d, *J* 16.5), 5.92 (1 H, s, C=C*H*), 7.28 (2 H, d, *J* 8, Ar-*H*), 7.66 (2 H, d, *J* 8, Ar-*H*); δ_C{¹H} (90MHz)(CDCl₃) 21.6 (*C*H₃), 39.8 (*C*H₂), 44.0 (*C*H), 47.7 (*C*H₂), 52.5 (*C*H₂), 126.2 (*C*H), 127.5 (*C*H), 130.1 (*C*H), 133.7 (C), 144.2 (C), 178.6 (C), 207.2 (C=O).

CLAIMS

- 1. Use of an immobilised transition metalcarbonyl complex as a catalyst in a Pauson-Khand reaction.
- 5 2. Use of an immobilised π -alkynetransition metalcarbonyl complex as a catalyst for the Pauson-Khand reaction.
 - 3. Use of a catalyst as claimed in claim 1 or 2 wherein the transition metal is selected from cobalt, rhodium, iridium, tungsten, molybdenum, titanium, nickel, iron and ruthenium.
 - 4. Use as claimed in claim 3 wherein the transition metal is cobalt.
- 10 5. A process for the preparation of a cyclopentenone compound or analogue thereof which comprises either;
 - reacting an alkyne, an alkene, and carbon monoxide in the presence of an immobilised transition metalcarbonyl catalyst; or
 - reacting an alkyne, an alkene, and carbon monoxide in the presence of an immobilised
- 15 alkynetransition metalcarbonyl catalyst.
 - 6. A process as claimed in claim 5 wherein the transition metal is selected from cobalt, rhodium, iridium, tungsten, molybdenum, titanium, nickel, iron and ruthenium.
 - 7. A process for the preparation of a resolved or partly resolved cyclopentenone compound or analogue thereof which comprises either;
- 20 reacting an alkyne, an alkene, and carbon monoxide in the presence of a resolved or partially resolved immobilised heterobitransition metalcarbonyl catalyst; or
 - reacting an alkyne, an alkene, and carbon monoxide in the presence of a resolved or partially resolved immobilised heterobitransition metalcarbonyl catalyst.
 - 8. A process as claimed in claim 7 wherein each transition metal is selected from cobalt,
- 25 rhodium, iridium, tungsten, molybdenum, titanium, nickel, iron and ruthenium.

COMBINED DECLARA		PLICATION AND POWI ENT OF COMMERCE Trademark Office	ER OF ATTORNEY
		ATTORNEY	DOCKET NO.: Z70582/UST
As a below named inventor, I hereb	y declare that:		
Alex Christian Comely, Sue	Elizabeth Gibson, Neil Jam	es Hales	
My residence, post office address a	nd citizenship are as stated below n	ext to my name,	
I believe I am the original, first and names are listed below) of the subje			
The specification of which the Title	: Catalyst For Pauson-Khand Rea	ction	
Is attached hereto; or			
Was filed as United States applicati	on Serial No on and	was amended on (if appl	icable); or
Was filed as PCT international appl PCT Article 19 On (if applicable).	ication Number PCT/GB00/03139	on 21 st August 2000 (21.08.200	0) and was amended under
I hereby state that I have reviewed a amended by any amendment referre		bove-identified specification, in	ncluding the claims, as
I acknowledge the duty to disclose to claims presented in this application	to the U.S. Patent and Trademark C in accordance with Title 37, Code of	office information, which is mat of Federal Regulations Section 1	erial to the Patentability of .56.
I hereby claim foreign priority bene application(s) for patent or inventor country other than the United States inventor's certificate or any PCT int filed by me on the same subject man	's certificate or Section 365(a) of an s of America listed below and have ternational application(s) designation	ny PCT international application also identified below any foreign at least one country other than	n(s) designating at least one gn applications(s) for patent or n the United States of America
PRIOR FOREIGN APPLICATION	(S):		
COUNTRY (If PCT, indicate PCT)	APPLICATION NUMBER	DATE OF FILING (Day, month, year)	PRIORITY CLAIMED
GB	9920296.2	27.08.1999	Yes
			Yes No
			Yes No
			Yes No

	Combined		cludes Reference to	Power of Attorney - (Continued) PCT International Applications) Y DOCKET NO.: Z70582/UST	
I hereby claim th application(s) lis		, United States Code	Section119 (e) of an	ny United States provisional	
	U.S. PRO	OVISIONAL APPLI	CATIONS		
U.S. PROVISIONAL AP	PLICATION NO.	U.S.	FILING DATE:		
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BENEFIT: U.S. OR PCT IN	PLICATIONS OR PCT I TERNATIONAL ATIONS		APPLICATIONS DI	ESIGNATING THE U.S. FOR	
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Combined Declaration for Patent Application and Power of Attorney - (Co	ntinued)
(Includes Reference to PCT International Appl	ications)
ATTORNEY DOCKET NO : 770	

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that

willful false statements and Title 18 of the United States application or any patent iss	s Code, and that such willful false state	e or imprisonment, or both, under Section 1001 of ements may jeopardize the validity of the	
FULL NAME OF SOLE OR FIRST INVENTOR	Alex Christian Comely		
RESIDENCE & CITIZENSHIP	Strand London	COUNTRY OF CITIZENSHIP United Kingdom	X
POST OFFICE ADDRESS	Kings College Strand London	WC2R 2LS GB	
FIRST OR SOLE INVENTOR	L'S SIGNATURE	DATE	
Alco Chitim		8.2.2002,	
FULL NAME OF SECOND INVENTOR	Sue Elizabeth Gibson		
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POST OFFICE ADDRESS	Kings College Strand London	1 WC2R 2LS GB	
SECONDANVENTOR'S SIGN	NATURE	DATE	
Silan E.	O. bra	15. 2.02.	
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